09/965,522 Search Strategy/Results

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     (FILE 'HOME' ENTERED AT 07:24:31 ON 30 MAY 2002)

     FILE 'MEDLINE, AGRICOLA, CAPLUS, BIOSIS, EMBASE, WPIDS' ENTERED AT
     07:24:39 ON 30 MAY 2002
L1      1911552 S ANTIBODY OR IMMUNOGLOBULIN OR IMMUNOGLOBIN OR IG#
L2        59785 S L1 AND (CHIMER? OR HUMANIZED OR FAB OR SCFV)
L3            6 S L2 AND (SODIUM (S) COTRANSPORTER)
L4            3 DUP REM L3 (3 DUPLICATES REMOVED)
L5           15 S L2 AND (SODIUM (S) (COTRANSPORTER OR CO-TRANSPORTER OR TRANS
L6           10 DUP REM L5 (5 DUPLICATES REMOVED)

=>
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=> d 1- ibib abs
YOU HAVE REQUESTED DATA FROM 10 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:315100 CAPLUS
DOCUMENT NUMBER: 136:336302
TITLE: Protein and cDNA sequences for novel human proteins and their use in diagnosis and disease treatment
INVENTOR(S): Edinger, Shlomit; Gerlach, Valerie; Macdougall, John R.; Malyankar, Uriel M.; Smithson, Glennda; Millet, Isabelle; Peyman, John A.; Stone, David J.; Gunther, Erik; Ellerman, Karen; Shimkets, Richard A.; Padigaru, Muralidhara; Guo, Xiaojia; Patturajan, Meera; Taupier, Raymond J.; Burgess, Catherine E.; Zerhusen, Bryan D.; Kekuda, Ramesh; Spytek, Kimberly A.; Gangolli, Esha A.; et al.
PATENT ASSIGNEE(S): Curagen Corporation, USA
SOURCE: PCT Int. Appl., 305 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002033087	A2	20020425	WO 2001-US32496	20011017

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2000-241040P P 20001017
US 2000-241058P P 20001017
US 2000-241063P P 20001017
US 2000-241243P P 20001017
US 2000-242152P P 20001020
US 2000-242482P P 20001023
US 2000-242611P P 20001023
US 2000-242612P P 20001023
US 2000-242880P P 20001024
US 2000-242881P P 20001024
US 2000-259028P P 20001229
US 2001-269813P P 20010220
US 2001-294108P P 20010425
US 2001-286324P P 20010529
US 2001-303698P P 20010709
US 2001-303968P P 20010709
US 2001-981151 A2 20011016

AB Disclosed herein are 10 nucleic acid sequences that encode novel polypeptides and their variants. The polypeptides show sequence homol. to zinc metalloproteases, ADAM-TS7, .alpha.2-macroglobulin, ileal **sodium**/bile acid **cotransporter**, prohibitin, macrophage stimulating protein, fatty acid-binding protein, gap junction .beta.5 protein, metallothionein, CIP4, hepsin/plasma transmembrane protein, and spinesin. Protein domains or motifs, tissue expression profiles, chromosomal mapping, and single nucleotide polymorphisms are provided. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or **antibody**. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L6 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:763183 CAPLUS
DOCUMENT NUMBER: 135:314469
TITLE: Protein and cDNA sequences of human GABA transporter 2 sequence homolog, and uses thereof in therapy, diagnosis, and drug screening
INVENTOR(S): Brandt, Silke
PATENT ASSIGNEE(S): Merck Patent G.m.b.H., Germany
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077321	A2	20011018	WO 2001-EP3916	20010406
WO 2001077321	A3	20020131		

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: EP 2000-107612 A 20000407

AB This invention provides protein and cDNA sequences for a newly identified human protein, which is belived to encode a novel member of GABA **transporter** 2-like protein, since it shows homol. with mouse **sodium**- and chloride-dependent GABA **transporter** 2 (GAT-2). In one embodiment, the invention relates to diagnostic assays for detecting diseases assocd. with inappropriate GABA transporter 2 sequence homolog activity or levels. Also disclosed are methods for utilizing sequence homolog in drug screening assays and in therapy directed against diseases assocd. with inappropriate GABA transporter 2 sequence homolog activity or levels.

L6 ANSWER 3 OF 10 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2001-607217 [69] WPIDS
DOC. NO. CPI: C2001-180417
TITLE: Preparation of functionalized polyalkyleneimine, for use in transfection of cells with nucleic acids, comprises treating polyalkyleneimine with functionalized hemiacetal in presence of titanium isopropoxide and sodium borohydride.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): HERSCOVICI, J; LECLERC, F; SCHERMAN, D; LECLERCQ, F
PATENT ASSIGNEE(S): (AVET) AVENTIS PHARMA SA; (HERS-I) HERSCOVICI J; (LECL-I) LECLERCQ F; (SCHE-I) SCHERMAN D
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001060890	A2	20010823	(200169)*	FR	23
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
FR 2805271	A1	20010824	(200169)		
US 2001031498	A1	20011018	(200169)		
AU 2001035695	A	20010827	(200176)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001060890	A2	WO 2001-FR460	20010215
FR 2805271	A1	FR 2000-2059	20000218
US 2001031498	A1 Provisional	US 2000-203907P	20000512
		US 2001-783981	20010216
AU 2001035695	A	AU 2001-35695	20010215

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001035695	A Based on	WO 200160890

PRIORITY APPLN. INFO: US 2000-203907P 20000512; FR 2000-2059 20000218

AN 2001-607217 [69] WPIDS
AB WO 200160890 A UPAB: 20011126
NOVELTY - Preparation of functionalized polyalkyleneimines (I) comprises treating a polyalkyleneimine (II) with a functionalized hemiacetal (III) in the presence of titanium (IV) isopropoxide and sodium borohydride.

DETAILED DESCRIPTION - Preparation of functionalized polyalkyleneimines of formula (I) comprises treating a polyalkyleneimine of formula (II) with a functionalized hemiacetal (III) in the presence of titanium (IV) isopropoxide and sodium borohydride.

R1-R4 = H, group compatible with the reaction (specifically OH, 1-4C alkyl or 1-4C hydroxyalkyl) or a targeting element (specifically selected from sugars, peptides, proteins, oligonucleotides, lipids, neuro-mediators, hormones, vitamins or their derivatives), provided that at least one targeting element is present;

R = H or -((CH2)n-NH)q-;

n = 2-10;

p, q = integers such that (p + q) gives (II) an average molecular weight of 102 to 107.

An INDEPENDENT CLAIM is included for a composition comprising (I) obtained as above and at least one nucleic acid (specifically DNA or RNA, especially where the nucleic acid contains one or more genes of interest under the control of regulation sequences).

USE - The process is useful for introducing targeting elements into (II), to give products (I) for use in nucleic acid formulations for transfection of target cells (e.g. particular types of cells or cell in particular types of tissues), in vitro or in vivo.

Use of (I)/nucleic acid compositions comprises preparation of cell transfection medicaments and the transfer of nucleic acids into cells; and a method for transferring nucleic acids into cells, comprising forming a (I)/nucleic acid composition and contacting the composition with the cells. Typically sense or antisense genes or genes encoding antigenic peptides (e.g. for vaccination) can be introduced for therapeutic purposes, e.g. in the treatment of mucoviscidosis, tumors or viral infections.

ADVANTAGE - The process is carried out in alcohol solvents compatible with (II) and uses non-toxic and relatively inexpensive reagents. In particular sodium borohydride is used instead of the highly toxic and much more expensive sodium cyanoborohydride.

Dwg.0/4

L6 ANSWER 4 OF 10 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-597722 [68] WPIDS
DOC. NO. CPI: C2001-176929
TITLE: Modulators of regulatory protein RS1, useful for treating diabetes or tumors and for increasing drug transport, control concentration of transport proteins in plasma membranes.
DERWENT CLASS: B04 D16
INVENTOR(S): KOEPSELL, H; KORN, T; KUEHLKAMP, T; TRACK, C; VEYHL, M
PATENT ASSIGNEE(S): (KOEP-I) KOEPSELL H
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 10006887	A1	20010906	(200168)*		22

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 10006887	A1	DE 2000-10006887	20000216

PRIORITY APPLN. INFO: DE 2000-10006887 20000216
AN 2001-597722 [68] WPIDS
AB DE 10006887 A UPAB: 20011121
NOVELTY - Compound (I) for regulating the concentration of transport proteins (TP) in the plasma membrane of cells that acts by modifying the activity or concentration of the regulatory protein RS1.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) expression vector containing a nucleic acid (II) that (i) encodes a ribozyme or antisense RNA, directed against mRNA of RS1, or an **antibody** against RS1, or (ii) encodes RS1 or its fragments; and

(2) cells that contain the vector of (1) or in which the RS1-encoding gene has been inactivated or deleted.

ACTIVITY - Antidiabetic; antitumor.

MECHANISM OF ACTION - Modulating the concentration or activity of RS1 which controls the concentration of TP and thus, indirectly, the uptake of nutrients and active ingredients by cells. Overexpression of RS1 reduces TP concentration, so causes death of (tumor) cells by starvation, and, by reducing glucose uptake, also reduces insulin demand.

LLC-PK1 epithelial cells were transfected with a vector that contained, in the antisense orientation, a fragment of RS1-encoding DNA that included the start codon and adjacent regions. The cells were tested for initial uptake of 14C-labeled alpha -methylglucopyranoside (AMG) in presence of 40 mu M AMG and of 80 mu M phlorizin. The phlorizin-inhibitable AMG transport rate in the cells was about 500 and 320 pmole/mg/min, in presence of 5 or 25 mM glucose, respectively. The corresponding values for wild-type cells were 30 and 130 pmole/mg/min, indicating that inhibition of RS1 resulted in increased **sodium** /glucose **co-transporter** activity. Cells transformed with RS1-encoding DNA in the sense orientation showed reduced AMG uptake (about 20-30% of wild-type).

USE - (I) that increase activity or concentration of RS1 are used to reduce or inhibit uptake of nutrients and/or active ingredients by cells, specifically of glucose for treatment of diabetes and tumors, while those that decrease RS1 activity are used to increase uptake, particularly of pharmaceuticals.

ADVANTAGE - Reducing expression of RS1 improves transport of pharmaceuticals into cells, particularly for delivering agents across the blood-brain barrier. Improved transport allows reduction in the size or frequency of doses, and thus of side-effects.

Dwg.0/13

L6 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:625037 CAPLUS
TITLE: Analysis of gene associated with exogenous nucleic acid improving repair of intestinal epithelium after .gamma. irradiation in mice
AUTHOR(S): Cui, Daxiang; Zeng, Guiying; Wang, Feng; Tian, Furong; Guo, Yanhai; Xu, Junrong; Yan, Xiaojun; Ren, Dongqing; Su, Chengzhi
CORPORATE SOURCE: Institute of Genetic Diagnosis, Fourth Military Medical University, Xi'an, 710033, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Jinzhan (2001), 28(3), 353-357
CODEN: SHYCD4; ISSN: 1000-3282
PUBLISHER: Shengwu Huaxue Yu Shengwu Wuli Jinzhan Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The mol. mechanism of exogenous nucleic acids improving repair of irradn.-damaged intestinal epithelium was studied. 45 mice being irradiated by .gamma. ray were treated with 40 .mu.g small intestinal RNA as test group, whose small intestinal specimens were collected resp. at 6 h, 12 h, 24 h, 4 d and 8 d after treatment; 40 mice being irradiated by .gamma. ray were treated with physiol. saline as control group, whose small intestinal specimens were collected at the same interval time. Then fragments of genes expressed in test group higher than those in control group, were obtained by using LD-PCR based on subtractive hybridization. After that, these gene fragments were cloned into T vectors, and were sequenced. Obtained sequences were searched for GenBank. 90 clones assocd. with repair of irradn.-damaged crypt cells were obtained. In test group of 6 h, higher similar sequences mainly were as follows: mRNA for heat shock protein, Nmi mRNA, Dutt1 protein, mRNA for Na, K-ATPase gamma subunit, mRNA for heat shock protein, finger type transcript factor, porcine growth hormone-releasing hormone gene, Homo sapiens dual specificity phosphatase, etc. In test group of 12 h, higher similar sequences were as follows: alk. phosphatase mRNA, alk. phosphatase 2, glkA gene, single stranded replicative centromeric gene, Homo sapiens DMBT1 candidate tumor gene, tRNA-Met gene, mouse **Ig** unrearranged transcribed H-chain, thyroxine-binding globulin gene, alpha-2- plasmin inhibitor gene. In test group of 24 h, higher similar sequences were as follows: anti-CEA **ScFv antibody** heavy chain vary region, anti-DNA **antibody Ig** heavy chain, mRNA for **Ig** kappa chain region, anti- BONT/A Hc **ScFv antibody** heavy chain vary region, mRNA for **ScFv** collagenase heavy chain vary region, AE0199 **Ig** heavy chain, mouse **Ig** gamma-chain, **Ig** rearranged gamma-chain mRNA, anti- NP **antibody IgH**, mRNA for arginine/serine kinase, dual specificity phosphatase, family mRNA telomerase-assocd. protein, anti-human erB-2 region, BMP-4 gene. In test group of 4 d, higher similar sequences were as follows: mRNA for **sodium** channel, tazarotene-induced gene, betaine- GABA **transporter** gene, homobox protein Xgbx-2 mRNA, mRNA for stress-activated protein, FK506 binding protein, calcium/calmodulin dependent gene, PEST phosphatase interactin gene, haptoglobin mRNA. In test group of 8 d, higher similar sequences were as follows: **Ig** Mu variable region mRNA, Mus musculus **Ig** K chain mRNA- V-region, mRNA for Hox1b protein, Mus musculus neutroactin mRNA, rat alk. phosphatase mRNA, Human mRNA for XP-C repair complementing protein, human alpha-2-plasmin inhibitor gene, mRNA for CCAT binding factor, mouse active H-chain VJ region, etc. Eighteen

were new sequences, whose function were unclear. Ninety clones were obtained to be assocd. with repair of damaged mice intestinal gland cells caused by .gamma. ray and treated by small intestinal RNA. Repair of damaged intestinal gland cells treated by exogenous nucleic acids may be assocd. with hsp, Nmi, Dutt1, alk. phosphatase genes and eighteen new sequences.

L6 ANSWER 6 OF 10 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-303738 [26] WPIDS
DOC. NO. CPI: C2000-092257
TITLE: Isolated, synthetic or recombinant chi-conotoxin peptide capable of inhibiting neuronal amine transporter used for treatment or prophylaxis of urinary or cardiovascular conditions, mood disorders, or treatment/control of pain/inflammation.
DERWENT CLASS: B04
INVENTOR(S): ALEWOOD, P F; LEWIS, R J; SHARPE, I A
PATENT ASSIGNEE(S): (UYQU) UNIV QUEENSLAND
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000020444	A1	20000413	(200026)*	EN	47

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 9964530	A	20000426	(200036)		
EP 1117682	A1	20010725	(200143)	EN	

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000020444	A1	WO 1999-AU844	19991001
AU 9964530	A	AU 1999-64530	19991001
EP 1117682	A1	EP 1999-952156	19991001
		WO 1999-AU844	19991001

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9964530	A	Based on	WO 200020444
EP 1117682	A1	Based on	WO 200020444

PRIORITY APPLN. INFO: AU 1998-6274 19981002
AN 2000-303738 [26] WPIDS
AB WO 200020444 A UPAB: 20000531
NOVELTY - An isolated, synthetic or recombinant chi-conotoxin peptide (P1) having the ability to inhibit a neuronal amine transporter, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated, synthetic chi-conotoxin peptide (P2) having the ability to inhibit a neuronal amine transporter having a sequence selected from (single letter amino acid code):
NGVCCGYKLCHOC;
VGVCCGYKLCHOC; or
(i) a sequence which has undergone one or more amino acid deletion, additions, substitutions or side chain modifications;

(2) an isolated nucleic acid molecule (N1) comprising a sequence of nucleotides encoding or complementary to a sequence encoding P1 or P2;

(3) a nucleic acid probe (N2)comprising a sequence of nucleotides encoding or complementary to a sequence encoding P1;

(4) a monoclonal or polyclonal **antibody** to P1; and

(5) a genetic construct comprising a vector portion and a nucleic acid capable of encoding P1.

ACTIVITY - Antiarrhythmic; cardiant; antidepressant; anxiolytic; analgesic; anti-inflammatory.

Chinese hamster ovary (CHO) cells were grown in 24 well plates (Falcon) in 10% v/v fetal calf serum. On reaching 60-70% confluence, the cells were transiently transfected (Lipofectamine, Gibco) with an expression vector (pcDNA3, Invitrogen) incorporating the full length cDNA for the human neuronal noradrenaline transporter (Pacholczyk et al., (1991) Nature, 350, 350-4). A cDNA clone of the neuronal noradrenaline transporter was used (Vollum Institute, Portland, OR, USA). Cellular uptake studies were performed 36 hours after transfection. The CHO cells were initially washed with transport buffer containing (mM): NaCI, 157; KCI, 2.7; NaH2PO4 11.8; MgCl2, 1.0 and CaCI2, 0.1; and of pH 7.4. The cells were then incubated with transport buffer containing 50 nM (3H)-noradrenaline (supplemented with unlabelled noradrenaline as required) and 100 micro M ascorbic acid. Chi-MrIA (0.1 nM-1 micro M) or desipramine (10 micro M) were also included as appropriate. After 20 minutes at room temperature, the cells were rapidly washed with ice cold phosphate buffered saline and then lysed in 0.1 % v/v Triton-X. The cell lysates were taken for liquid scintillation counting to determine their level of radioactivity. Additionally, an aliquot of the cell lysate was used to measure protein concentration (BioRad DC protein assay). The specific uptake of (3H)-noradrenaline by the noradrenaline transporter was defined as the component sensitive to desipramine (10 micro M).

The accumulation of noradrenaline into CHO cells expressing the human neuronal noradrenaline transporter was reduced to less than 0.5% of the control amount by desipramine (10 micro M), demonstrating that the accumulation was due almost entirely to specific uptake via the cloned transporter. The noradrenaline transporter was confirmed as the target of the conotoxin in cellular uptake studies. Chi-MrIA (0.1 nM-1 micro M) inhibited the accumulation of radiolabeled noradrenaline in a concentration-dependent manner, with a log inhibitory concentration (IC)50 value of -8.17 plus or minus 0.0275 (n = 4). The concentration of chi-MrIA

required to inhibit the accumulation by 50% was found to be approximately 7 nM. This concentration is approximately one order of magnitude lower than that needed for desipramine to produce the same effect.

Cocaine and chi-MrIA are both naturally occurring compounds, however, they are quite dissimilar. Cocaine is an alkaloid extracted from the leaves of the coca plant, whereas chi-MrIA is a peptide directly encoded by an animal gene. In addition to its effect at the uptake **transporter**, cocaine is known to possess potent local anaesthetic properties. This is due to blockade of both **sodium** and potassium channels. No evidence was found for local anaesthetic activity of chi-MrIA in any of the assays. It was found that chi-MrIA had neither contractile nor relaxant effects on the tone of the vas deferens by itself. Similar studies revealed that chi-conotoxin does not inhibit the dopamine **transporter**.

MECHANISM OF ACTION - Inhibition of the neuronal noradrenaline transporter.

USE - The peptides are useful for the treatment or prophylaxis of urinary or cardiovascular conditions or diseases (arrhythmia or coronary heart failure) or mood disorders (depression, anxiety or cravings), or the treatment or control of pain or inflammation (chronic pain, neuropathic pain or inflammatory pain).

Dwg.0/5

L6 ANSWER 7 OF 10 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-256979 [22] WPIDS
DOC. NO. NON-CPI: N2000-191026
DOC. NO. CPI: C2000-078548
TITLE: Neutral amino acid **transporter** protein which conjugates with cell membrane protein 4F2 and operates independently of **sodium** ions is useful for screening potential cancer proliferation inhibitors.
DERWENT CLASS: B04 D16 P14
INVENTOR(S): ENDOU, H; KANAI, Y
PATENT ASSIGNEE(S): (NISC-N) JAPAN SCI & TECHNOLOGY CORP; (KAGA-N) KAGAKU GIJUTSU SHINKO JIGYODAN
COUNTRY COUNT: 23
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000014228	A1	20000316	(200022)*	JA	189
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA US					
AU 9954487	A	20000327	(200032)		
JP 2000157286	A	20000613	(200035)		68
EP 1111048	A2	20010627	(200137)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000014228	A1	WO 1999-JP4789	19990903
AU 9954487	A	AU 1999-54487	19990903
JP 2000157286	A	JP 1999-248546	19990902
EP 1111048	A2	EP 1999-940648	19990903
		WO 1999-JP4789	19990903

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9954487	A	Based on	WO 200014228
EP 1111048	A2	Based on	WO 200014228

PRIORITY APPLN. INFO: JP 1999-248546 19990902; JP 1998-249993 19980903
AN 2000-256979 [22] WPIDS
AB WO 200014228 A UPAB: 20000508

NOVELTY - A cell surface protein (LAT1), which mediates the transport of neutral amino acids, leucine, isoleucine, phenylalanine, methionine, tyrosine, tryptophan, valine and histidine, into the cell independently of sodium ions, is new. The protein conjugates with the cell membrane surface molecule 4F2.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) peptides including a partial LAT1 sequence;
(2) DNA encoding LAT1;
(3) RNA corresponding to the DNA of (2);
(4) expression vectors containing the DNA of (2);
(5) host cells transformed by the vectors of (4);
(6) monoclonal and polyclonal antibodies and antisera reacting with LAT1;
(7) cells expressing the monoclonal antibodies of (6);
(8) drug compositions containing sense or antisense DNA or RNA encoding or antisense to LAT1, or the antibodies of (6);
(9) a method for the assay of LAT1 in biological samples using the antibodies of (6);
(10) kits for the assays of (9);
(11) a method for screening potential inhibitors of the transport of neutral amino acids, by contacting with LAT1 and selecting for binding; and
(12) transgenic mice expressing LAT1.

ACTIVITY - Anticancer.

MECHANISM OF ACTION - LAT1 antagonists.

USE - The antisense DNA or RNA, antibodies, **antibody** fragments, and peptide and non-peptide antagonists to LAT1 are useful as anticancer agents.

DESCRIPTION OF DRAWING(S) - The drawing shows the degree of transport of 14-C labelled leucine into Xenopus oocytes 2 and 5 hours from injection of cRNA encoding (left to right) LAT1, 4F2hc, both LAT1 and 4F2hc, and neither (control). Leucine transport is much greater in cells treated with both LAT1 and 4F2hc.

Dwg.4/28

L6 ANSWER 8 OF 10 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000198202 MEDLINE
DOCUMENT NUMBER: 20198202 PubMed ID: 10731661
TITLE: Ganglioside GT1b in rat brain binds to p58, a brain-specific **sodium**-dependent inorganic phosphate **cotransporter**: expression cloning with a specific monoclonal **antibody** to ganglioside GT1b-binding protein.
AUTHOR: Kotani M; Tajima Y; Shimoda Y; Irie A; Kubo H; Tai T
CORPORATE SOURCE: Departments of Tumor Immunology, Biochemical Cell Research, and Membrane Biochemistry, The Tokyo Metropolitan Institute of Medical Science, Honkomagome Bunkyo-ku, Tokyo 113-8613, Japan.. kotani@rinshoken.or.jp
SOURCE: JOURNAL OF BIOCHEMISTRY, (2000 Jan) 127 (1) 13-22.
Journal code: HIF; 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000427
Last Updated on STN: 20000928
Entered Medline: 20000414

AB To evidence the notion that gangliosides involve neuronal cell interactions in the brain, we surveyed the presence of ganglioside-binding proteins in membrane lysates of adult rat cerebellum. Three proteins (p58, p90, and p160) were identified as GT1b-binding proteins by incubation of the blot of the membrane lysate with GT1b micelles. We generated a monoclonal **antibody** (mAb) specific to the polypeptide portion of the GT1b-binding proteins (YAK-2). The YAK-2 mAb specifically reacted with all three proteins on blots of proteins pretreated under nonreducing conditions for SDS-PAGE, but reacted mainly with p58 under reducing conditions, showing that p90 and p160 are oligomeric forms of p58. The binding activity of the YAK-2 mAb was completely inhibited by the presence of GT1b micelles, indicating the specificity of YAK-2 mAb for p58 and its oligomers. Immunohistochemical investigations revealed that both p58 and GT1b colocalize within the granular layer of adult rat cerebellum. Expression cloning of p58 cDNA was performed using YAK-2 mAb, and five putative clones were obtained. Among them, the nucleotide sequence of one cDNA completely matched that of rat brain-specific **sodium**-dependent inorganic phosphate **cotransporter** (rBNPI), a 61 kDa membrane protein. COS7 cells were transfected with a Flag-**chimeric** construct containing the rBNPI/p58 cDNA, and the membrane lysate was subjected to immunoprecipitation with anti-Flag **antibody**. One protein (64 kDa) was detected only with YAK-2 mAb, and the membrane lysate specifically bound to GT1b micelles. Taking together, we propose that rBNPI/p58 functions as a GT1b-binding protein in neuronal cells.

L6 ANSWER 9 OF 10 MEDLINE
ACCESSION NUMBER: 1999032641 MEDLINE
DOCUMENT NUMBER: 99032641 PubMed ID: 9815035
TITLE: Sorting of rat liver and ileal sodium-dependent bile acid transporters in polarized epithelial cells.
AUTHOR: Sun A Q; Ananthanarayanan M; Soroka C J; Thevananther S; Shneider B L; Suchy F J
CORPORATE SOURCE: Department of Pediatrics, Mount Sinai School of Medicine, New York, New York 10029, USA.
CONTRACT NUMBER: DK-34989 (NIDDK)
HD-20632 (NICHD)
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Nov) 275 (5 Pt 1) G1045-55.
Journal code: 3U8; 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981214

AB The rat ileal apical Na+-dependent bile acid transporter (ASBT) and the liver Na+-taurocholate cotransporting polypeptide (Ntcp) are members of a new family of anion transporters. These transport proteins share limited sequence homology and almost identical predicted secondary structures but are localized to the apical surface of ileal enterocytes and the sinusoidal surface of hepatocytes, respectively. Stably transfected Madin-Darby canine kidney (MDCK) cells appropriately localized wild-type ASBT and Ntcp apically and basolaterally as assessed by functional activity and immunocytochemical localization studies. Truncated and **chimeric** transporters were used to determine the functional importance of the cytoplasmic tail in bile acid transport activity and membrane localization. Two cDNAs were created encoding a truncated transporter in which the 56-amino-acid COOH-terminal tail of Ntcp was removed or substituted with an eight-amino-acid epitope FLAG. For both mutants there was some loss of fidelity in basolateral sorting in that approximately 75% of each protein was delivered to the basolateral surface compared with approximately 90% of the wild-type Ntcp protein. In contrast, deletion of the cytoplasmic tail of ASBT led to complete loss of transport activity and sorting to the apical membrane. An Ntcp **chimera** in which the 56-amino-acid COOH-terminal tail of Ntcp was replaced with the 40-amino-acid cytoplasmic tail of ASBT was largely redirected (82.4 +/- 3.9%) to the apical domain of stably transfected MDCK cells, based on polarity of bile acid transport activity and localization by confocal immunofluorescence microscopy. These results indicate that a predominant signal for sorting of the Ntcp protein to the basolateral domain is located in a region outside of the cytoplasmic tail. These studies have further shown that a novel apical sorting signal is localized to the cytoplasmic tail of ASBT and that it is transferable and capable of redirecting a protein normally sorted to the basolateral surface to the apical domain of MDCK cells.

L6 ANSWER 10 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92316845 MEDLINE

DOCUMENT NUMBER: 92316845 PubMed ID: 1352281
TITLE: Mouse-human **chimeric antibody** MH171 against the multidrug transporter P-glycoprotein.
AUTHOR: Ariyoshi K; Hamada H; Naito M; Heike Y; Seimiya H; Maezawa K; Tsuruo T
CORPORATE SOURCE: Cancer Chemotherapy Center, Japanese Foundation for Cancer Research, Tokyo.
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1992 May) 83 (5) 515-21.
Journal code: HBA; 8509412. ISSN: 0910-5050.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920815
Last Updated on STN: 19950206
Entered Medline: 19920806

AB We have developed a mouse-human **chimeric antibody** MH171, in which the antigen-recognizing variable regions of the mouse monoclonal **antibody** MRK17 are joined with the constant regions of human IgG1 antibodies. The MRK17 recognizes specifically the multidrug **transporter** P-glycoprotein and inhibits the growth of human multidrug resistant (MDR) tumor cells in vitro and in the xenograft nude mouse model system. The established **chimeric** MH171 **antibody** forms an apparently intact **IgG** composed of heavy and light chains covalently assembled via disulfide bonds in **sodium** dodecyl sulfate polyacrylamide gel electrophoresis analysis and is specific to MDR cell lines with a similar affinity to the original mouse MRK17. MH171 also displays strong **antibody**-dependent cell-mediated cytotoxicity to the target cells in vitro, when human mononuclear cells are used as effector cells. The **chimeric** **antibody** against P-glycoprotein, MH171, should be a useful agent in the treatment of human drug-resistant tumors.

	Hits	Search Text
1	1	6245887.pn.
2	2354	antibody with (chimeric and fab)
3	486	antibody with (chimeric and fab and (single adj chain) and humanized)
4	31	(antibody with (chimeric and fab and (single adj chain) and humanized)) and transporter
5	435	(antibody with (chimeric and fab and (single adj chain) and humanized)) and purification
6	33	(antibody with (chimeric and fab and (single adj chain) and humanized)) and immunopurification
7	1087	single adj chain adj antibody
8	51	(single adj chain adj antibody) and (immunoglobulin adj library)

	L #	Hits	Search Text
1	L1	2	"9118294"
2	L2	7	"9118294"
3	L3	1	5872237.pn.